Parathyroid storm: rare manifestation of primary hyperparathyroidism

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Parathyroid storm can be fatal if not recognized early. We describe the clinical course and management of a patient in whom this condition presented as severe hypercalcemia and hypernatremia.

Case report

A confused 65-year-old man was admitted to another hospital because of anorexia, polyuria, weakness and a weight loss of 4.5 kg over a 3-week period. His past history was unremarkable.

There were no abnormal physical findings, but the serum levels of creatinine, calcium and phosphorus were abnormal, at 595 (normally less than 120) μmol/L, 4.53 (normally 2.20 to 2.60) mmol/L and 1.76 (normally 0.85 to 1.45) mmol/L respectively. After 4 days of therapy with intravenously administered fluids and furosemide the calcium level fell to 3.46 mmol/L, but the patient remained confused. The serum levels of sodium and chloride were high, at 160 (normally 135 to 145) and 117 (normally 96 to 106) mmol/L respectively; the levels of potassium and carbon dioxide were normal, at 4.7 (normal values 3.5 to 5.0) and 29 (normal values 22 to 30) mmol/L respectively. The patient was transferred to our hospital.

The patient was disoriented and appeared chronically ill. His central venous pressure was 3 cm H_2O, blood pressure 100/70 mm Hg and pulse rate 60 beats/min. He was afebrile. The serum creatinine level had fallen to 468 μmol/L. The serum magnesium level was 0.73 (normally 0.70 to 1.06) mmol/L and the serum albumin level 26 (normally 35 to 50) g/L. Urinalysis showed nothing abnormal.

The patient was treated with 0.9% saline and 20 mg of methylprednisolone, administered intravenously, every 6 hours. Once the central venous pressure was normal the 0.9% saline was replaced with 0.45% saline plus boluses of normal saline to maintain the central venous pressure at 8 to 10 cm H_2O, and 40 mg of furosemide was given every 8 hours to ensure a urine output of 200 mL/h. The patient's mental status improved, the serum sodium level fell to normal, and the serum creatinine level fell to 273 μmol/L. However, since the serum calcium level remained elevated, at 2.91 mmol/L, 200 MRC units of calcitonin was given subcutaneously every 8 hours and 2 g of phosphate given orally three times daily. This was insufficient to reduce the calcium level below 2.60 mmol/L.

The serum alkaline phosphatase level was 209 (normally 20 to 100) U/L and the proportion of bone isoenzyme elevated. A skeletal roentgenographic survey that included the hands was normal, as was serum protein electrophoresis (aside from a low albumin level). A bone scan showed increased uptake in the lungs, stomach, knees and ankles. Complete gastrointestinal investigation, intravenous pyelography, and a liver and spleen scan were normal, as was the 24-hour urinary excretion of protein. A bone marrow biopsy showed resorptive lacunae containing osteoclasts and fibrosis, suggestive of osteitis fibrosa cystica. Computerized tomography revealed a mass on the left side of the neck inferolateral to the thyroid cartilage, and the parathyroid hormone level was found to be 1260 (normally 29 to 85) pmol/L.

A parathyroid adenoma measuring 3.5 × 2.5 × 1.2 cm was removed from the left side of the neck. Three normal parathyroid glands were identified. The serum calcium level fell to 2.39 mmol/L the day after surgery and is still normal; the patient remains well.

Discussion

This patient had severe hypercalcemia, which led to poor oral intake of fluids, a urinary concentrating defect and renal insufficiency, resulting in hypernatremia and contraction of the extracellular fluid volume. The hypernatremia and volume contraction were likely also related to the excessive use of furosemide relative to the amount of saline infused.

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Initially the patient was treated with 0.9% saline despite hypernatremia in order to expand the extracellular fluid volume as rapidly as possible and thus improve calcium excretion. In such cases it is of paramount importance that the extracellular fluid volume be returned to normal and kept so while furosemide is given since insufficient volume replacement can lead to increased hypernatremia and increased tubular reabsorption of calcium. Since idiogenic osmoles are generated within brain cells in hypertonic states to prevent brain cell dehydration, too rapid lowering of the serum sodium level can cause cerebral edema; therefore, the subseqent reduction of the patient's serum sodium level was gradual. The serum electrolyte and magnesium levels should be closely monitored in this situation and deficits corrected.

The terms acute hyperparathyroidism, parathyroid crisis and parathyroid storm have been used to designate this rare fulminant presentation of primary hyperparathyroidism. In their recent review Bayat-Mokhtari and colleagues[1] found 128 cases in the world literature since 1939, when the first case was reported.[2] Wang and Guyton[3] noted that 14 (1.6%) of 882 patients treated surgically for primary hyperparathyroidism had parathyroid storm, presenting with marked mental disturbances and very high serum calcium and parathyroid hormone levels; 40% had renal calculi then or had had them in the past. It is unclear why mild hypercalcemia should progress to the crisis state, with such a profound rise in the serum calcium level, but contraction of the extracellular fluid volume, stress from intercurrent medical illness, or hemorrhage within an intact gland could be precipitating factors.[4]

Without an appropriate history, differentiating parathyroid storm from hypercalcemia associated with malignant disease is difficult. Distinguishing features of the latter are chronically ill appearance, anemia, hypoalbuminemia and absence of skeletal changes associated with hyperparathyroidism,[3] although in our patient the presence of some of these features led us to suspect malignant disease at first. A bone scan showing uptake of the radioactive isotope in the lungs and stomach that can be attributed to metastatic calcification may suggest primary or secondary hyperparathyroidism rather than malignant disease.[1,5] In addition to ultrasonography, computerized tomography has been used to demonstrate parathyroid adenomas; its variable success rate has recently improved to as much as 78% in some series.[6]

Pathological studies of parathyroid glands in these patients usually show a single chief-cell adenoma and only rarely carcinoma or hyperplasia, although electron microscopy has shown many lysosomal bodies, this reflecting a high level of synthesis and release of hormone.[7]

Definitive treatment is resection of the tumour. While the diagnosis is being sought, aggressive medical therapy to control the hypercalcemia and the fluid and electrolyte status should be instituted. Failure of medical treatment, even in the presence of coma, is an indication for emergency surgical exploration if sufficient evidence is present to exclude malignant disease.[4]

In the case we have presented, the diagnosis of parathyroid storm was not made for almost 2 weeks after admission. With the availability of computerized tomography, ultrasonography and rapid assays for parathyroid hormone in some institutions, we suggest early assessment of the parathyroid glands in cases of severe hypercalcemia to establish the diagnosis and expedite definitive management, for if parathyroid storm is not recognized early the outcome can be fatal.

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References

1. Bayat-Mokhtari F, Palmieri GMA, Moinuddin M et al: Parathyroid storm. *Arch Intern Med* 1980; 140: 1092–1095
2. Hanes EM: Hyperparathyroidism due to parathyroid adenoma with death from parathormone intoxication. *Am J Med Sci* 1939; 197: 85–90
3. Wang CA, Guyton SW: Hyperparathyroid crisis: clinical and pathologic studies of 14 patients. *Ann Surg* 1979; 190: 782–790
4. Maselly MJ, Lawrence AM, Brooks M et al: Hyperparathyroid crisis. Successful treatment of ten comatose patients. *Surgery* 1981; 90: 741–746
5. Davis BA, Poulose KP, Reba RC: Scanning for uremic pulmonary calcifications [C]. *Ann Intern Med* 1976; 85: 132
6. Stark DD, Moss AA, Gooding GAW et al: Parathyroid scanning by computed tomography. *Radiology* 1983; 148: 297–298
7. Hehrmann R, Thiele J, Tidow G et al: Acute hyperparathyroidism. Clinical, laboratory and ultrastructural findings in a variant of primary hyperparathyroidism. *Klin Wochenschr* 1980; 58: 501–510

Chemistry without catalysis

Chemistry without catalysis, would be a sword without a handle, a light without brilliance, a bell without sound.

—Alwyn Mittasch (1869–1953)